

SEQUENCE LISTING

<110> Crooke, Stanley T.
 Lima, Walter
 Wu, Hongjiang

<120> Methods of Using Mammalian RNase H and Compositions Thereof

<130> ISPH-0520

<140> US/09/781,712

<141> 2001-02-12

<150> US 09/684,254

<151> 2000-10-06

<150> US 09/343,809

<151> 1999-06-30

<150> US 09/203,716

<151> 1998-12-02

<150> US 60/067,458

<151> 1997-12-04

<160> 39

<170> PatentIn version 3.0

<210> 1

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<212> PRT

<213> Homo sapiens

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Val Asp Glu Ala Gly Arg Gly Pro Val Leu Gly Pro Met Val Tyr Ala 35 40 45

Ile Cys Tyr Cys Pro Leu Pro Arg Leu Ala Asp Leu Glu Ala Leu Lys 50 55 60

Val Ala Asp Ser Lys Thr Leu Leu Glu Ser Glu Arg Glu Arg Leu Phe
65 70 75 80

Ala Lys Met Glu Asp Thr Asp Phe Val Gly Trp Ala Leu Asp Val Leu 85 90 95

Ser Pro Asn Leu Ile Ser Thr Ser Met Leu Gly Trp Val Lys Tyr Asn 100 105 110

Leu Asn Ser Leu Ser His Asp Thr Ala Thr Gly Leu Ile Gln Tyr Ala 115 120 125

Leu Asp Gln Gly Val Asn Val Thr Gln Val Phe Val Asp Thr Val Gly 130 135 140

Met Pro Glu Thr Tyr Gln Ala Arg Leu Gln Gln Ser Phe Pro Gly Ile 145 150 155 160

Glu Val Thr Val Lys Ala Lys Ala Asp Ala Leu Tyr Pro Val Val Ser 165 170 175

Ala Ala Ser Ile Cys Ala Lys Val Ala Arg Asp Gln Ala Val Lys Lys 180 185 190

Trp Gln Phe Val Glu Lys Leu Gln Asp Leu Asp Thr Asp Tyr Gly Ser 195 200 205

Gly Tyr Pro Asn Asp Pro Lys Thr Lys Ala Trp Leu Lys Glu His Val 210 215 220

Glu Pro Val Phe Gly Phe Pro Gln Phe Val Arg Phe Ser Trp Arg Thr 225 230 235 240

Ala Gln Thr Ile Leu Glu Lys Glu Ala Glu Asp Val Ile Trp Glu Asp 245 250 255

Ser Ala Ser Glu Asn Gln Glu Gly Leu Arg Lys Ile Thr Ser Tyr Phe 260 265 270

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Ile Cys Tyr Cys Pro Leu Ser Arg Leu Ala Asp Leu Glu Ala Leu Lys 50 55 60

Val Ala Asp Ser Lys Thr Leu Thr Glu Asn Glu Arg Glu Arg Leu Phe 65 70 75 80

Ala Lys Met Glu Glu Asp Gly Asp Phe Val Gly Trp Ala Leu Asp Val . 85 90 95

Leu Ser Pro Asn Leu Ile Ser Thr Ser Met Leu Gly Arg Val Lys Tyr 100 105 110

Asn Leu Asn Ser Leu Ser His Asp Thr Ala Ala Gly Leu Ile Gln Tyr 115 120 125

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Val Leu Gly Ile Asp Glu Ala Gly Arg Gly Pro Val Leu Gly Pro Met 35 40 45

Val Tyr Ala Ala Ile Ser Pro Leu Asp Gln Asn Val Glu Leu Lys 50 55 60

Asn Leu Gly Val Asp Asp Ser Lys Ala Leu Asn Ġlu Ala Lys Arg Glu 65 70 75 80

Glu Ile Phe Asn Lys Met Asn Glu Asp Glu Asp Ile Gln Gln Ile Ile 85 90 95

Ala Tyr Ala Leu Arg Cys Leu Ser Pro Glu Leu Ile Ser Cys Ser Met
100 105 110

Leu Lys Arg Gln Lys Tyr Ser Leu Asn Glu Val Ser His Glu Ala Ala 115 120 125

Ile Thr Leu Ile Arg Asp Ala Leu Ala Cys Asn Val Asn Val Glu 130 135 140

Ile Lys Val Asp Thr Val Gly Pro Lys Ala Thr Tyr Gln Ala Lys Leu 145 150 155 160 Glu Lys Leu Phe Pro Gly Ile Ser Ile Cys Val Thr Glu Lys Ala Asp 165 170 175

Ser Leu Phe Pro Ile Val Ser Ala Ala Ser Ile Ala Ala Lys Val Thr 180 185 190

Arg Asp Ser Arg Leu Arg Asn Trp Gln Phe Arg Glu Lys Asn Ile Lys 195 200 205

Val Pro Asp Ala Gly Tyr Gly Ser Gly Tyr Pro Gly Asp Pro Asn Thr 210 215 220

Lys Lys Phe Leu Gln Leu Ser Val Glu Pro Val Phe Gly Phe Cys Ser 225 230 235 240

Leu Val Arg Ser Ser Trp Lys Thr Ala Ser Thr Ile Val Glu Lys Arg 245 250 . 255

Cys Val Pro Gly Ser Trp Glu Asp Asp Glu Glu Glu Gly Lys Ser Gln 260 265 270

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Pro Met Val Tyr Ala Val Ala Tyr Ser Thr Gln Lys Tyr Gln Asp Glu 50 55 60

Thr Ile Ile Pro Asn Tyr Glu Phe Asp Asp Ser Lys Lys Leu Thr Asp 65 70 75 80

Pro Ile Arg Arg Met Leu Phe Ser Lys Ile Tyr Gln Asp Asn Glu Glu 85 90 95

Leu Thr Gln Ile Gly Tyr Ala Thr Thr Cys Ile Thr Pro Leu Asp Ile

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Thr Val Ala Lys Lys Ala Asp Ser Leu Tyr Cys Met Val Ser Val Ala 180 185 190

Ser Val Val Ala Lys Val Thr Arg Asp Ile Leu Val Glu Ser Leu Lys 195 200 205

Arg Asp Pro Asp Glu Ile Leu Gly Ser Gly Tyr Pro Ser Asp Pro Lys 210 215 220

Thr Val Ala Trp Leu Lys Arg Asn Gln Thr Ser Leu Met Gly Trp Pro 225 230 235 240

Ala Asn Met Val Arg Phe Ser Trp Gln Thr Cys Gln Thr Leu Leu Asp 245 250 255

Asp Ala Ser Lys Asn Ser Ile Pro Ile Lys Trp Glu Glu Gln Tyr Met 260 265 270

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Leu Ser Glu Lys Arg Arg Leu Ala Leu Tyr Glu Glu Ile Lys Glu Lys
50 55 60

Ala Leu Ser Trp Ser Leu Gly Arg Ala Glu Pro His Glu Ile Asp Glu 65 70 75 80

Leu Asn Ile Leu His Ala Thr Met Leu Ala Met Gln Arg Ala Val Ala 85 90 95

Gly Leu His Ile Ala Pro Glu Tyr Val Leu Ile Asp Gly Asn Arg Cys100 105 110

Pro Lys Leu Pro Met Pro Ala Met Ala Val Val Lys Gly Asp Ser Arg 115 120 125

Val Pro Glu Ile Ser Ala Ala Ser Ile Leu Ala Lys Val Thr Arg Asp 130 135 140

Ala Glu Met Ala Ala Leu Asp Ile Val Phe Pro Gln Tyr Gly Phe Ala 145 150 155 160

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His Gly Ala Thr Glu His His Arg Arg Ser Phe Gly Pro Val Lys Arg 180 185 190

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<213> Homo sapiens

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<302> Human Type 2 RNase H

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<311> 1998-12-02

<312> 1999-12-14

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Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Lys Lys Phe Ala Thr Glu 50 55 60

Asp Glu Ala Trp Ala Phe Val Arg Lys Ser Ala Ser Pro Glu Val Ser 65 70 75 80

Glu Gly His Glu Asn Gln His Gly Gln Glu Ser Glu Ala Lys Pro Gly
85 90 95

Lys Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Gln
100 105 110

Pro Tyr Ala Lys His Met Lys Pro Ser Val Glu Pro Ala Pro Pro Val 115 120 125

Ser Arg Asp Thr Phe Ser Tyr Met Gly Asp Phe Val Val Val Tyr Thr 130 135 140

Asp Gly Cys Cys Ser Ser Asn Gly Arg Arg Lys Pro Arg Ala Gly Ile 145 150 155 160

Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu 165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Lys 180 185 190

Ala Ile Glu Gln Ala Lys Thr Gln Asn Ile Asn Lys Leu Val Leu Tyr 195 200 205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Gln Gly 210 215 220

Trp Lys Lys Asn Gly Trp Lys Thr Ser Ala Gly Lys Glu Val Ile Asn 225 230 235 240

Lys Glu Asp Phe Val Ala Leu Glu Arg Leu Thr Gln Gly Met Asp Ile 245 250 255

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<301> Wu et al.

<302> Molecular Cloning and Expression of cDNA for Human RNase H

<303> Antisense Nucleic Acid Drug Design

<304> 8

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<306> 53-61

<307> 1998-02-08

<308> AF039652

<309> 1998-04-02

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Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Lys Lys Phe Ala Thr Glu 50 55 60

Asp Glu Ala Trp Ala Phe Val Arg Lys Ser Ala Ser Pro Glu Val Ser 65 70 75 80

Glu Gly His Glu Asn Gln His Gly Gln Glu Ser Glu Ala Lys Ala Ser 85 90 95

Lys Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Glu 100 105 110

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Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu 165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Lys 180 185 190

Ala Ile Glu Gln Ala Lys Thr Gln Asn Ile Asn Lys Leu Val Leu Tyr 195 200 205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Gln Gly 210 215 220

Trp Lys Lys Asn Gly Trp Lys Thr Ser Ala Gly Lys Glu Val Ile Asn 225 230 235 240

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<301> Cerritelli and Crouch

<302> Cloning, Expression and Mapping of Ribonucleases H of Human and Mouse Related to Bacterial RNase HI

<303> Genomics

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<306> 300-307

<307> 1998-11-01

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Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Lys Lys Phe Ala Thr Glu
50 60

Asp Glu Ala Trp Ala Phe Val Arg Lys Ser Ala Ser Pro Glu Val Ser 65 70 75 80

Glu Gly His Glu Asn Gln His Gly Gln Glu Ser Glu Ala Lys Ala Ser

Lys Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Glu 100 105 110 Pro Tyr Ala Lys His Met Lys Pro Ser Val Glu Pro Ala Pro Pro Val 115 120 125

(algorith)

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Asp Gly Cys Cys Ser Ser Asn Gly Arg Arg Pro Arg Ala Gly Ile 145 150 155 160

Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu 165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Lys 180 185 190

Ala Ile Glu Gln Ala Lys Thr Gln Asn Ile Asn Lys Leu Val Leu Tyr 195 200 205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Gln Gly 210 215 220

Trp Lys Lys Asn Gly Trp Lys Thr Ser Ala Gly Lys Glu Val Ile Asn 225 230 235 240

Lys Glu Asp Phe Val Ala Leu Glu Arg Leu Thr Gln Gly Met Asp Ile 245 250 255

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<213> Homo sapiens

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<301> Frank, Braunshofer-Reiter, Poltl and Holzmann

<302> Cloning, Subcellular Localization and Functional Expression of Human RNase HII

<303> Biol. Chem.

<304> 379

<305> 99

<306> 1407-1412

<307> 1998-12-01

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Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Lys Lys Phe Ala Thr Glu 50 55 60

Asp Glu Ala Trp Ala Phe Val Arg Lys Ser Ala Ser Pro Glu Val Ser 65 70 75 80

Glu Gly His Glu Asn Gln His Gly Arg Glu Ser Glu Ala Lys Ala Ser 85 90 95

Lys Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Glu 100 105 110

Pro Tyr Ala Lys His Met Lys Pro Ser Val Glu Pro Ala Pro Pro Val 115 120 125

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Asp Gly Cys Cys Ser Ser Asn Gly Arg Arg Arg Pro Arg Ala Gly Ile 145 150 155 160

Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu 165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Lys 180 185 190

Ala Ile Glu Gln Ala Lys Thr Gln Asn Ile Asn Lys Leu Val Leu Tyr 195 200 205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Arg Gly
210 215 220

Trp Lys Lys Asn Gly Trp Lys Thr Ser Ala Gly Lys Glu Val Ile Asn 225 230 235 240

Lys Glu Asp Phe Val Ala Leu Glu Arg Leu Thr Gln Gly Met Asp Ile 245 250 255

Gln Trp Met His Val Pro Gly His Ser Gly Phe Ile Gly Asn Glu Glu 260 265 270

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<301> Frank, Braunshofer-Reiter, Wintersberger, Grimm and Busen

<302> Cloning of the cDNA encoding the large subunit of human RNase HI, a homologue of the prokaryotic RNase HII

and the group of the engineering against

<303> Proc. Natl. Acad. Sci. USA

<304> 95

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<307> 1998-10-27

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Ile Cys Tyr Cys Pro Leu Pro Arg Leu Ala Asp Leu Glu Ala Leu Lys 50 55 60

Val Ala Asp Ser Lys Thr Leu Leu Glu Ser Glu Arg Glu Arg Leu Phe 70 75 80

Ala Lys Met Glu Asp Thr Asp Phe Val Gly Trp Ala Leu Asp Val Leu 85 90 95

Ser Pro Asn Leu Ile Ser Thr Ser Met Leu Gly Arg Val Lys Tyr Asn 100 105 110

Leu Asn Ser Leu Ser His Asp Thr Ala Thr Gly Leu Ile Gln Tyr Ala 115 120 125

Leu Asp Gln Gly Val Asn Val Thr Gln Val Phe Val Asp Thr Val Gly 130 135 140

Met Pro Glu Thr Tyr Gln Ala Gln Leu Gln Gln Ser Phe Pro Gly Ile 145 150 155 160

Glu Val Thr Val Lys Ala Lys Ala Asp Ala Leu Tyr Pro Val Val Ser 165 170 175

Ala Ala Ser Ile Cys Ala Lys Val Ala Arg Asp Gln Ala Val Lys Lys 180 185 190

Trp Gln Phe Val Glu Lys Leu Gln Asp Leu Asp Thr Asp Tyr Gly Ser

195 200 205

Gly Tyr Pro Asn Asp Pro Lys Thr Lys Ala Trp Leu Lys Glu His Val 210 215 220

Glu Pro Val Phe Gly Phe Pro Gln Phe Val Arg Phe Ser Trp Arg Thr 225 230 235 240

Ala Gln Thr Ile Leu Glu Lys Glu Ala Glu Asp Val Ile Trp Glu Asp 245 . 250 . 255

Ser Ala Ser Glu Asn Gln Glu Gly Leu Arg Lys Ile Thr Ser Tyr Phe 260 265 270

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<302> Cloning, Expression and Mapping of Ribonucleases H of Human and Mouse Related to Bacterial RNase HI

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<307> 1998-11-01

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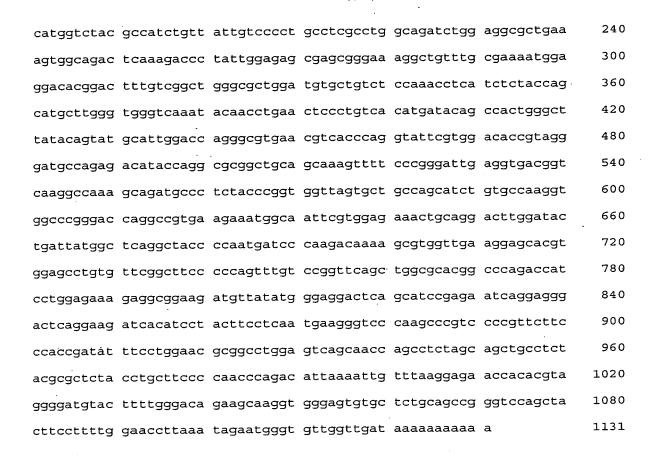
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Lys	Arg	Pro	Arg 100	Glu	Pro	Leu	Gly	Glu 105	Gly	Glu	Glu	Leu	Pro 110	Glu	Pro
Gly	Pro	Lys 115	His	Thr	Arg	Gln	Asp 120	Thr	Glu	Pro	Ala	Ala 125	Val	Val	Ser
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Val	Tyr	Trp	Gly	Pro 165	Gly	His	Pro	Leu	Asn 170	Val	Gly	Ile	Arg	Leu 175	Pro
Gly	Arg	Gln	Thr 180	Asn	Gln	Arg	Ala	Glu 185	Ile	His	Ala	Ala	Cys 190	Lys	Ala
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Glu	Asp	Phe	Met	Glu 245	Leu	Asp	Glu	Leu	Thr 250	Glņ	Gly	Met	Asp	Ile 255	Gln
Trp	Met	His	Ile 260	Pro	Gly	His	Ser	Gly. 265	Phe	Val	Gly	Asn 	Glu 270	Glu	Ala
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